

| <u>DB Name</u> | <u>Query</u> | <u>Hit Count</u> | <u>Set Name</u> |
|----------------|---|------------------|-----------------|
| USPT | (modified or mutated) same (FRAP or FK506 or cyclophilin or calcineurin) same inhibit\$ same T adj cells | 0 | <u>L12</u> |
| USPT | (FRAP or FK506 or cyclophilin or calcineurin) same inhibit\$ same T adj cells | 76 | <u>L11</u> |
| USPT | (FRAP or FK506 or cyclophilin or calcineurin) same inhibit\$ | 340 | <u>L10</u> |
| USPT | L5 and L6 and L7 | 0 | <u>L9</u> |
| USPT | L5 and L6 | 60 | <u>L8</u> |
| USPT | inhibition same proliferation same T adj cells | 217 | <u>L7</u> |
| USPT | (modified or mutated or changed) same macrolide | 60 | <u>L6</u> |
| USPT | macrolide | 1320 | <u>L5</u> |
| USPT | macrolide adj binding adj protein | 0 | <u>L4</u> |
| USPT | T adj cells same (MBP or macrolide adj binding adj protein) same (inhibit or stop or preven) same proliferation | 6 | <u>L3</u> |
| USPT | mutated adj (MBP or macrolide adj binding adj protein) | 0 | <u>L2</u> |
| USPT | T adj cells same (MBP or macrolide adj binding adj protein) same proliferation | 40 | <u>L1</u> |

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| (modified or mutated) same (FRAP or FK506 or cyclophilin or calcineurin) same inhibit\$ same T adj cells | 0 |

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Search History**Today's Date: 8/2/2000**

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L11: Entry 4 of 76

File: USPT

Apr 18, 2000

DOCUMENT-IDENTIFIER: US 6051398 A

TITLE: Nucleic acids encoding CR3 polypeptide, vector and transformed cell thereof, and expression thereof

DEPR:

The ligand-activated genes are then screened in the library using any one of several different methods. One method involves differential hybridization with cDNA probes constructed from mRNA derived from ligand-activated cells and unactivated cells. Another method includes hybridization subtraction, whereby cDNA from ligand-activated cells is hybridized with an excess of mRNA from unactivated cells to remove RNA molecules common to both. Alternatively, cDNA probes can be made from the same pool of thiol-selected mRNA used to make the cDNA library, as these sequences are highly enriched for ligand-induced molecules. One can prepare cDNA probes from mRNA extracted from cells treated with drugs that block the biologic response to the particular cytokine (e.g., rapamycin blocks the proliferative response of T cells to IL-2, and cyclosporin A and FK506 block the T-cell response to activation via the T-cell antigen receptor). Results from probing with the cDNA made from drug-inhibited cells can then be compared to results from probes made from cells not inhibited by these drugs.

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L11: Entry 2 of 76

File: USPT

Jun 6, 2000

DOCUMENT-IDENTIFIER: US 6071883 A

TITLE: Flavone analogues useful as anti-rejection agents

BSPR:

Over 25 new immunosuppressants are currently under investigation for the treatment or prevention of allograft reactions, and many are already in clinical trials. Each drug has advantages and limitations. CsA and its analogues, for example cyclosporin G and tacrolimus (EK506) are T-cell early activation inhibitors. These drugs block T-cell early activation at the Go/G1 interface and are largely specific for T cells or T-dependent functions initiated through the T-cell receptor complex. In its side effects, EK506 resembles CsA, with regard to nephrotoxicity, neurotoxicity, and hyperglycaemia. CsA also causes hirsutism and gingival hyperplasia (see the aforementioned Groth et al. and Sorel et al.).

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L11: Entry 10 of 76

File: USPT

Jan 11, 2000

DOCUMENT-IDENTIFIER: US 6013641 A

TITLE: Use of hyaluronic acid as an immunosuppressant

BSPR:

Immunosuppressants such as cyclosporin A, FK506, rapamycin and azathioprine have been used to prevent graft rejection, and to treat some forms of autoimmune disease. However, they have numerous side effects. There is therefore substantial interest in identifying new agents that can inhibit the activation of specific cells, particularly T cells, while having fewer side effects.

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L7: Entry 1 of 217

File: USPT

Aug 1, 2000

DOCUMENT-IDENTIFIER: US 6096305 A

TITLE: Receptor that binds IL-17

DEPR:

Soluble IL-17R/Fc significantly inhibited the mitogen-induced proliferation of purified murine splenic T cells in a dose dependent manner, while a control Fc had no effect on the murine T cell proliferation. Complete inhibition of mitogen induced proliferation was observed at a soluble IL-17R.Fc concentration of 10 .mu.g/ml. Analysis of IL-2 production by splenic T cells activated with Con A in the presence or absence of IL-17R.Fc in the culture revealed that addition of IL-17R.Fc to the T-cell culture inhibited IL-2 production to levels 8-9-fold lower than those observed in cultures containing media alone or media plus a control Fc protein. Similar results were observed when purified human T cells were used.

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L5: Entry 1 of 1320

File: USPT

Aug 1, 2000

DOCUMENT-IDENTIFIER: US 6096785 A

TITLE: Amino acid compositions and use thereof in treating renal dysfunction

BSPR:

Ascomycins, of which FK-506 is the best known, are another class of generally immunosuppressive substances, also referred to as macrolide immunosuppressants. FK-506 is a macrolide immunosuppressant that is produced by *Streptomyces tsukubaensis* No. 9993. The structure of FK-506 is given in the appendix to The Merck Index, supra, as item A5. A large number of related compounds which retain the basic structure and immunological properties of FK-506 are also known. These compounds are described in various publications, for example EP 184162, EP 315973, EP 323042, EP 423714, EP 427680, EP 465426, EP 474126, WO 91/13889, WO 91/19495, EP 484935, EP 532088, EP 532089, WO 93/5059 and the like. Ascomycin, FK-506 and their structurally similar analogues and derivatives as well as metabolites thereof are termed collectively "ascomycins" in this specification.

DEPR:

The dosage should be such that the medicaments or nutritional formulations are effective for the prevention and/or treatment of nephrotoxicity induced by macrolide immunosuppressive drugs.

DEPR:

The supplement will conveniently be administered in the form of unit doses suitable for administration of the supplement 1 to 4 times per day. Where the diets of the invention comprise energy sources, it is appropriate not to supply more than 1000 Kcal/day. Apart from this limitation with respect to the energy supply, diet supplements of the invention for preventing and/or treating nephrotoxicity induced by macrolide immunosuppressive drugs can and will conveniently be supplied in the form of formula diets as described above.

DEPR:

Typical pharmacologically acceptable formulation forms for oral administration will further comprise pharmacologically acceptable diluents, carriers, vitamins, spices, pigments and/or other adjuvants well known to the skilled person to be suitable for incorporation into such formulation and optionally a macrolide immunosuppressive drug.

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L6: Entry 1 of 60

File: USPT

Apr 25, 2000

DOCUMENT-IDENTIFIER: US 6054435 A

TITLE: 6-O-substituted macrolides having antibacterial activity

BSTL:

| | |
|---------------------------------|-------------------------|
| | Erythromycin R' R' ' |
| | A --OH --CH.sub.3 B --H |
| --CH.sub.3 C --OH --H D --H --H | |

and are well-known and potent antibacterial agents. These compounds are used widely to treat and prevent bacterial infection. As with other antibacterial agents, however, bacterial strains having resistance or insufficient susceptibility to erythromycin have been identified. Erythromycin A has only weak activity against Gram-negative bacteria. Therefore, there is a continuing need to identify new macrolide compounds which possess improved antibacterial activity, which have less potential for developing resistance, which possess the desired Gram-negative activity, and/or which possess unexpected selectivity against target microorganisms. Consequently, numerous investigators have prepared chemical derivatives of erythromycin in an attempt to obtain analogs having modified or improved profiles of antibiotic activity.

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L1: Entry 1 of 40

File: USPT

Aug 1, 2000

DOCUMENT-IDENTIFIER: US 6096776 A

TITLE: Green porphyrins as immunomodulators

DEPR:

Splenocytes prepared as described in paragraph 1 of this example, when cultured with 100 .mu.g/ml of MBP, generate a proliferative response by expansion of T cells specific for, and activated by, MBP. This proliferative response is indexed at 100% in comparison with cells cultured in the absence of MBP which is indexed at 0%. When the cells are cultured in the presence of BPD at concentrations of 1 ng/ml-1 .mu.g/ml, the proliferation is inhibited. At 1 ng/ml of BPD the proliferation is only 20%; the index falls to zero at 10 ng/ml. At over 100 ng/ml, the proliferative response is less than that seen in the cells cultured in the absence of MBP.